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THE COMPARATIVE MORPHOLOGY, TAXONOMY, AND DISTRIBUTION OF THE MYRICACEÆ OF THE EASTERN UNITED STATES.*

By HEBER W. YOUNGKEN, Ph.D.

Along the eastern seaboard of the United States there occur five good species of *Myricaceæ,* and a hybrid between two of these.

Myrica cerifera, Linne, varies from a low shrub to a tree 12 metres high, and extends northward, contrary to past statements, as far as Tuckahoe, New Jersey. The writer finds this species to be strictly evergreen and wholly confined to coastal regions within sight of the sea.

Myrica Caroliniensis, Miller, with which the previous named species has often been confounded, is strictly deciduous, except when strong basal shoots are formed. The leaves on these may be sub-evergreen.

The lanceolate leaves of *Myrica cerifera* drop without assuming a copper-red color. The elliptic-obovate leaves of *Myrica Caroliniensis* assume a greenish-brown hue on an extensive scale in October and November, previous to leaf-fall. This species is of wide distribution along the coastal plain, and even ascends to 1200 feet at Mount Desert.

A hybrid between the two above species, *Myrica Macfarlanei,* Youngken, is frequent where both parents abound. Its characteristics follow:

Root (secondary structure).—The hybrid root resembles both parents in respect to its cork, its cells containing gummy lignin. *Actinomyces* in ducts, barred septa and crystal fibres accompany-

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ing the hard bast. It resembles *M. Caroliniensis* in the number of primary medullary rays and in having comparatively broad medullary ray cells. It differs from both parents by having larger intercellular air-spaces in the cortex, more crystals of calcium oxalate in both cortex and phloem, broader and more numerous sclerenchyme elements in cortex, and narrower tracheæ. The primary medullary rays are 1–6, occasionally 1–7, rows of cells in width.

Stem (gross structure).—A shrub rising to a height of 2 to 2.5 metres, with very crooked branches, the younger of which frequently appear stunted in habit. The shoots of the first year's growth are somewhat intermediate in nature with those of *M. cerifera* and *M. Caroliniensis*. They are of a greenish- to reddish-brown color, more thin hairy than those of *M. cerifera*, somewhat less hairy than those of *M. Caroliniensis*, but showing numerous yellow and a few orange-red glandular hairs. Upon them appear the buds of next season's leaves and flowers. The branchlets of two years' growth are dull reddish brown and devoid of thin hairs, but possess a few golden-yellow glands. Lenticels are present which vary from 0.5 to 0.7 mm. in length and are arranged longitudinally. Alike with similar branchlets of *M. cerifera* and *M. Caroliniensis*, staminate or pistillate flowers are borne on special catkin axes, which, in the case of the pistillate, persist for a long time after the fruits have fallen. The writer observed these also present on stems of the third, fourth, and fifth year's growth at Wildwood, New Jersey, January 31, 1915. The older stems are brownish gray to ash gray color and have numerous circular to oval somewhat raised lenticels arranged both longitudinally and transversely, and varying from 0.5 to 1.5 mm. in length. The crooked underground stem creeps through the soil for long distances and gives off numerous branches. These send up tufts of spreading suckers at different nodes which frequently serve to propagate the species. These suckers grow downward and then upward in arcuate fashion. They are of a whitish to reddish-white aspect when recently dug up.

Aërial Stem (histology).—The aërial stem of the hybrid resembles that of *M. cerifera* in the following structure details: (*a*) A continuous sclerenchyme zone in the pericycle; (*b*) the tendency of the phloem masses to become arched in their outer portions, due to the broadening out of the medullary rays at their extremities; (*c*) the presence of many bast-fibres accompanied by crystal fibres as

well as stone cells in the phloem; (*d*) the uniformity in distribution of the tracheæ. It resembles the aërial stem of *M. Caroliniensis* in the size and relative number of tracheæ found in the protoxylem. It differs from both parents as follows: The autumnal wood is intermediate in thickness; the pitted tracheæ are fewer than in *M. cerifera,* more numerous than in *M. Caroliniensis;* the mean diameter of the tracheæ is intermediate between that of both parents. The primary medullary rays are 1–3, rarely 1–4, rows of cells wide; the secondary, 1–2 rows in width. Other stem structures common to both parents are likewise seen in the hybrid.

Subterranean Branch (histology).—Compared with the aërial stem of the same age, it shows fewer cork layers and a broader cortex. The cells of the cortex are generally larger, less angular, and contain more starch grains. The bast-fibres of the phloem are about twice as numerous and in larger groups. The tracheæ are fewer and generally broader, while the woody fibres are more numerous and more lignified. The pith is narrower, its elements smaller and more lignified. The primary medullary rays are broader and frequently show 1–5, less often 1–6, rows of cells in width. The secondary medullary rays vary in width from 1–2 to 1–3 rows of cells. Cortical parenchyme, phloem, and tracheal elements with a gummy lignin content are more frequent than in the above-ground stem. Compared with the rhizomes of its parents, it shows intermediate characters in respect to the number and mean diameter of the tracheæ and woody fibres.

Leaves (gross structure).—The leaves of this hybrid show several striking macroscopic characters which are intermediate between those of its parents. For instance, they vary from lanceolate-cuneate to elliptic-obovate in shape, many of them being a mean between these two forms. In duration they are semi-evergreen, and usually fall during February and March, by which time they have often assumed a slight coppery tint. In size they vary from 25 to 58 mm. in length and from 8 to 20 mm. in width. They have numerous orange-red and golden-yellow glandular hairs on their lower surface, with merely a few of each of these on their upper surface. (*M. cerifera* leaves have numerous orange-red and golden-yellow glandular hairs on both surfaces, while the leaves of *M. Caroliniensis* are devoid of orange-red glandular hairs, have numerous golden-yellow glandular hairs on their lower surface, and a mere scattering of these on their upper surface). Simple hairs are found on both surfaces and margin, as on the leaves of *M. Caroliniensis,* but relatively fewer in number. The

texture of the leaves is sub-coriaceous. In color the leaves have blended the color characteristics of both parents. The margin is more incurved beneath than *M. Caroliniensis,* less than *M. Cerifera.*

Leaf Histology.—The microscopic characters of the leaf of this hybrid are intermediate between those of its parents. For instance, the upper epidermis is composed of cells whose vertical walls are more curvilinear than *M. cerifera,* less curvilinear than *M. Caroliniensis.* Their mean dimensions in surface view are 26.7μ × 16.89μ. Their outer walls are less projecting than those of *M. cerifera,* more so than *M. Caroliniensis.* The cuticle is thinner than that of *M. cerifera,* thicker than that of *M. Caroliniensis.* The palisade region of the mesophyll is 3–4 layers wide, and so is intermediate between this region in *M. cerifera* and *M. Caroliniensis.* The lower epidermis consists of cells whose vertical walls are more curvilinear than those of *M. cerifera,* less curvilinear than those of *M. Caroliniensis.* The mean dimensions of these cells in surface view are 26.46μ × 13.59μ which is likewise an intermediate character. The stomata are fewer in number than on *M. Caroliniensis,* more numerous than on *M. cerifera.* The upper surface shows a scattering of orange-red, bowl-shaped glands and golden-yellow balloon-shaped glands, or sometimes the latter only. The lower surface shows numerous orange-red, bowl-shaped and golden-yellow, balloon-shaped glands, both of which are often fewer than on the similar epidermis of *M. cerifera.* The tendency for the head of the bowl-shaped gland in the hybrid to become saucer-shaped is very striking. Simple unicellular trichomes and the sclerotic bases of these are common on both lower and upper epidermis, but intermediate in number between those on the leaves of the parents. Finally, the average thickness of the lamina of the hybrid outside of the mid-rib is 201.6μ, while that of *M. cerifera* is 268.8μ and of *M. Caroliniensis,* 168.96μ.

Inflorescence and *Flowers.*—The characteristic inflorescence is a catkin. The catkins are partly formed the year before flowering below the leaves on last season's growing branches. The staminate catkins are borne on different plants from those which bear the pistillate catkins, and so the plants are diœcious. Both staminate and pistillate catkins possess orange-red, bowl- to saucer-shaped and golden-yellow, balloon-shaped glands on the catkin axis as well as the bracts. Other characters are still under investigation by the writer.

Fruits.—The hybrid fruits are ceriferous nuts which are intermediate in size, apex, weight, and duration between those of *M. ceri-*

fera and *M. Caroliniensis.* Their diameter varies from 3 to 4 mm. The apex of each mature fruit is pitted. Two hundred fruits which the writer gathered at Palermo, New Jersey, November 7, 1914, weighed 6.7 Gms. The fruits of one season past and several of the previous season adhere to the persistent catkin axes.

Myrica Gale, Linne, is distributed through northern regions, from Labrador and Newfoundland as far south as Warren County, New Jersey; from the Atlantic to the Pacific, and in eastern mountain regions to Virginia. Its leaves are strictly deciduous.

Myrica inodora, Bartram, from the statement of authors, is evergreen. In height and aspect it somewhat resembles *M. cerifera. Comptonia asplenifolia,* Aiton, is distributed from Nova Scotia to Saskatchewan, and southward to North Carolina and Tennessee. Its leaves are strictly deciduous.

Seedlings are for the first time described and figured from the cotyledonary stage onward for *M. cerifera, M. Caroliniensis,* and *M. Macfarlanei.* Their comparative morphology has been traced. The author shows that from the seedling primary root of five to six months' growth, and from thence onward, characteristic root tubercles are formed on *M. cerifera, M. Caroliniensis, M. Macfarlanei,* and *Comptonia asplenifolia.* The organism is found in all these to be an *Actinomyces* (which was isolated according to Koch's postulates in pure culture, first described by the writer and named by him *Actinomyces Myricarum*) that abundantly fills infested cells in the cortex of the tubercles, which owe their origin as arrested and modified roots to its irritant and invading action. As a result of cultures made from tubercles, the author concludes that good cultures of the organism can be secured in the depth of nutrient agar.[1]

Since *Actinomyces* is frequently a virulent pathogenic organism in cattle and other domestic animals up to man, because the swellings it produces on plants are analogous to those on animals, since the forms of the organism as shown by Jordan in the infested lesions of animals are similar to those which the writer has described in the lesions of *Myrica;* and since the cultural characteristics of the organism isolated from the lesions of animals by Wright, Wolff, and Israel are in many respects similar to those isolated from the *Myricas* and described by the writer, he would regard the organism as a parasite and suggest

[1] The writer has recently been successful in growing *Actinomyces Myricarum* on coagulated horse serum in sealed tubes kept at a temperature of 37.5° C.

its possible pathogenic relation to such animals. The *Actinomyces* not only confines itself to the cortex of the tubercular roots; it later works its way into the tracheæ of those structures, passes into the pitted vessels of the main roots, thence into those of the stems, and, conveyed by the transpiration stream gradually upward, is carried through the axes of catkins so as finally to reach the flowers, bracts, and fruits. In these it confines its existence to the part corresponding to the mediocortex of the root tubercles; namely, the mesophyll and outer mesocarp regions respectively. It has been observed by the writer in its most luxuriant form in the cells of the middle fruit wall of the various species studied. Here it can be recognized best in thin hand sections stained with safranin and methyl green in the form of rosettes, almost filling the cell lumina. When the fruits fall to the ground and subsequently break open their walls, the organism probably makes its way from the infected cells into the soil, where it spreads through wide areas, infecting the roots and stems of other Myricas and producing characteristic lesions.

In *Comptonia asplenifolia,* while *Actinomyces Myricarum* is the primary infecting agent responsible for the tubercles, there often appears in older tubercles a mycelium-producing fungus with non-septate hyphæ probably belonging to the Oomycetes.

As for the roots, so for the stems of *M. cerifera, M. Caroliniensis, M. Gale* and *Comptonia asplenifolia,* a careful histological study has been made and details recorded.

In the study of the leaves various new structural details have been observed, but special interest attaches to the presence now recorded of orange-red, bowl- to saucer-shaped glandular hairs specifically characteristic of *M. cerifera* and in a reduced degree of *M. Macfarlanei,* intermingled with golden-yellow glandular hairs of Chevalier. The latter only are present in *M. Caroliniensis.*

Exact phytophenological records have been made as to the maturation of the floral parts and the period of blossoming in April and May. Spore mother-cell formation is completed by autumn of one year, but formation of tetrads proceeds in the different species studied from mid-April to mid-May in the Philadelphia neighborhood.

Careful study has been made by the writer of stages in the development of the fruits of *M. cerifera, M. Caroliniensis,* and *M. Macfarlanei.* These will be described as one category, seeing that they closely agree with each other.

In early June the maturing wall of each ovary has already de-

veloped a series of striking and complex glandular hairs of the nature of the tubercular emergences. Each is a knob-like expansion of the fruit wall into which a copious prolongation of subjacent mesocarp tissue has spread, but farther, from an abundant and densely anastomosing complex of vascular bundles that ramify through the outer half of the maturing mesocarp, fine vascular diverticula, composed of two or three spiral tracheæ, along with delicate, elongated, seive-like elements, pass through the stalk of the emergences and end in a slight swelling in its middle. The epidermis at this time is comparatively shallow and thin-walled, while from the junction of the epidermis with the base of each emergence elongated unicellular hairs spring which form a basket-like system round and upon which copious wax exudations subsequently become aggregated.

At this time the mesophyll is divisible into two recognized zones, viz, an outer irregular and large-celled region consisting of about 12 or 13 layers, and an inner smaller and more round-celled tissue of more numerous layers. Prolonged into the former from the point of attachment of the fruit with the axis is a vascular tissue that on entering the outer layer ramifies abundantly and, as above stated, gives off delicate diverticula to the different emergences. At this time only slight indication is observed of a difference in cell contents, between the outer and the inner zone. The endocarp is a shallow and delicate layer that from now on becomes less and less conspicuous.

By mid-June, or soon thereafter, striking changes begin to appear. The epidermis, as well as the mesophyll cells of the emergences the general epidermal (epicarp) cells of the fruit wall and the outer zone of the mesocarp have all enlarged steadily and become filled up with an abundant secretion which assumes a bizarre coloration when stained with safranin and methyl green. Tints varying from neutral gray through pink, crimson, crimson-green, green-blue, yellow, and brown are all present in distinct but neighboring cells, and, though the writer has as yet been unable to apply abundant tests, the above coloration suggests the formation and presence already of the palmitic myristic, and stearic acids already tested for and recorded by pharmacists and synopsized by Chevalier.

At this time the inner layer of the mesocarp contracts conspicuously with the last, its cells remaining small, thin-walled, rounded, and its cavities filled with delicate protoplasm. A further stage in the maturation of the fruits is noted by the middle or latter part of July. Each knob-shaped emergence has developed around itself an

abundant waxy layer which, by hardening, gives a bluish-white color to the fruit surface. The mesophyll cells of these hairs, as well as 3 to 6 of the innermost cell layers of the outer zone, become loaded with cell contents that assume a uniform red or reddish-green hue which even heightens the bizarre coloration noted above. By this time, also, the cells of the inner zone have become largely thickened from within outward by lignified thickening and the cells themselves, having increased greatly in size and become markedly sinuous in outline, assume a bright red staining with safranin.

The thickening process clearly proceeds in centrifugal fashion, for in mid- or late July the inner walls, surrounding the ovarian cavity, may be highly lignified and stained a bright red hue, while as yet the external cells adjacent to the outer zone are little, if at all, altered in shape or lignified. Progressive lignification of this area gives rise by mid-August to the extremely hard scleroid fruit layers that efficiently protect the enclosed seed.

Meanwhile steady excretion of wax takes place over the cells of each emergence, and these later have so grown together as to form a complete coating around the fruit wall proper. So between the abundant wax excretion and the close apposition of the wax-secreting emergences the entire surface of each emergence assumes a uniform blue-gray color, and is coated over by a rather brittle waxy investment that readily crumples to pieces when slightly pressed between the fingers. This investment forms an admirable defensive covering alike against intense insulation, the attack of fungoid spores, and the destructive action of caterpillars and other animal enemies.

New and more exact taxonomic descriptions than have hitherto been submitted by authors are presented, and, in particular, the diagnostic characters of *M. cerifera, M. Caroliniensis,* and their hybrid have been fully elucidated.

SOME HISTORICAL AND BIBLIOGRAPHICAL NOTES ON THE THERAPEUTICS AND CHEMISTRY OF THE OXYPINENES.

By J. Emile Blomén, A.M., Ph.D.

Since my article on the oxypinenes appeared in the May number of this Journal I have received numerous inquiries regarding the chemistry of the *pinene-ozonide* in particular and other oxypinenes

in general. This must be my excuse for again touching on their chemistry in an article which I had promised should deal only with the therapeutical history of the oxypinenes.

Of all oxypinenes—by which term are understood all pinene compounds containing oxygen in some form or other—the ozonide is undoubtedly the most interesting, since from this form are developed the peroxides, aldehydes, ketones, and acids of pinene. Whenever oxidation or oxidation products of organic substances of ozone and its chemistry is mentioned, our mind reverts to the great chemist Schoenbein, the discoverer of this puzzling allotropic modification of the element oxygen, without which life could not be sustained.

Christian Friederich Schoenbein was born in Metzingen, Würtemberg, October 18, 1799; studied chemistry under the most celebrated chemists of his time, and became professor of chemistry in Basel, where he proved himself one of the most industrious and resourceful chemists of his age. He has written not less than 337 scientific treatises. Besides his discovery of ozone, his invention of gun cotton is best known. This later eventually became the basis for the photographic film, the celluloid, the artificial leather and silk, and the smokeless powder industries. He died in Wildbad, August 29, 1868.

In 1839, while investigating the relations between electrical and chemical forces, following the lead of the great Swedish chemist Jöns Jacob Berzelius in this line, Schoenbein discovered a new modification of oxygen, to which he gave a distinct name, "ozone"—the word being derived from the Greek ὀσω, "I smell," thereby indicating one of its most notable characteristics, which is that, in contradistinction to the ordinary oxygen, which is perfectly odorless, it has a very strong and peculiar odor. (For a full account of Schoenbein's discovery see *Smithsonian Institution's Report*, p. 166, 1864.)

Schoenbein's work was received with little favor by the scientific world, but he was not dismayed, and he contined his experiments for almost thirty years. The results of his labors can be found in *Comptes rendus . . . de l'Académie des Science,* Paris, for 1840–69.

Before considering the action on animal tissues of the two strongest oxidizers known, ozone and peroxide of hydrogen, and particularly of the most important of the oxy-products of pinene—the ozonide of pinene—it will be necessary to mention Schoenbein's work on them at some length.

Schoenbein found that if a few drops of acetate of lead are

added to dilute peroxide of hydrogen, or if ozonized oil of turpentine is shaken with this lead salt, peroxide of lead is formed. If, however, in the first case the peroxide of lead thus formed remains in contact with the peroxide of hydrogen, both are reduced, resulting in water, protoxide of lead, and oxygen.

From this Schoenbein concluded that the oxygen in the peroxide of hydrogen and the lead salt exists in opposite condition of purity, thus $H_2O.\overset{+}{O}$ and $PbO.\overset{-}{O}$, and that by union of these molecules ordinary inactive oxygen, $\overset{+}{O}.\overset{-}{O}$, is formed. Schoenbein called those bodies containing negatively active oxygen (or $\overset{-}{O}$) "ozonides," and all such bodies as peroxide of hydrogen ($H_2O\ \overset{+}{O}$), barium oxide ($BaO.\overset{+}{O}$), and all oxygen compounds which contained oxygen in a positively active condition, "antozonides." This form of oxygen he called "antozone."

From this we may draw the conclusions, first, that ozone and peroxide of hydrogen and ozone can not exist together—a fact which was definitely proved by Schoene in 1879,[1] and, secondly, that ozone can not be absorbed or held in solution by water, but will gradually oxidize this to peroxide of hydrogen, which again, in contact with oxidizable substances, will liberate positively active oxygen and reform water.

The importance of these deductions lies in the fact that when an ozonide such as pinene ozonide meets a moist surface such as the moist animal tissue the result must necessarily be the formation of peroxide of hydrogen and an oxy-compound containing molecular oxygen, and when the peroxide meets anything capable of being oxidized by positive oxygen it will give up one atom of positively active oxygen and form water.

On these reactions is the therapeutic value of pinene ozonide founded, and we may now return to the consideration of this compound, for, as was pointed out in my previous article, turpentine is one of the best ozone carriers known. This was very forcibly brought out by Chas. W. Wetherill in an article which appeared in the *Smithsonian Institution Report,* 1864, p. 174, and following, where he—besides the quotation in my previous article—also states: "Upon

[1] *Annalen,* vol. 196.

the animal organization ozonized oil of turpentine acts more energetically than oil not ozonized."

Since turpentine, when exposed to air, always absorbs ozone and oxygen, forming ozonide and other oxypinenes, it is safe to say that when the therapeutical value of turpentine is discussed—particularly in the older literature, to which the absorbing property of turpentine was unknown—this value, in equal or even higher degree, pertains to the oxypinenes.

The oxidation of turpentine in sunlight was first mentioned by Sobrero in 1851.[2] Later, H. E. Armstrong, in the course of his studies on the terpenes and camphor, became interested in the experiments of Sobrero and reached the same conclusion as he, that " when turpentine is exposed to sunlight in the presence of moisture and oxygen a crystalline substance is formed, which has a composition represented by the formula $C_{10}H_{16}O_2$, and that this substance is decomposed when boiled with dilute sulphuric acid, an oil being formed which has a powerful odor, resembling both that of camphor and that of turpentine."

This product, which was named " Sobrerol " in honor of Sobrero, is probably always the initial product of oxidation of turpentine.[3]

Sobrerol can also be prepared from a cold solution of pinene in acetic acid by the action of mercuric acid, but if a heated solution is used the resulting oxidation product is hydroxylketone.

The turpenes have been used for therapeutical purposes as early as the time of Hippocrates, and they were extensively employed by the ancients. Pliny appears to have recommended them in many diseases and Aretæus was also an enthusiastic advocate of their use. Ever since then the turpentines have continued to keep their place in medical practice.[4]

Although the ancients knew nothing of ozone and its absorption by pinene, and that until 1840 nothing had been heard of this life-giving substance, it had, of course, existed since the beginning of time and been conducive to the health of man.

The distilled oil of turpentine first made its appearance in the pharmaceutical literature in the latter part of the seventeenth century. In the Augsburg Pharmacopœia of 1648 are given the directions for its preparation, under the title " Oleum Terebenthina."

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[2] *Compt. rend.*, vol. 33, p. 66.

[3] *Jour. Chem. Soc.*, London, 1890.

[4] *Med. and Phys. Jour.*, London, vol. 46, p. 186.

In 1678 there appeared a published account of oil of turpentine in a little book by James Yonge, of Plymouth, where he describes its use for arresting hemorrhages. His book bears the title "Currus Triumphalis, e Terebintho; or an account of the many admirable virtues of the oleum therebenthinæ, etc., in two letters, the one to James Pearce, Esq., Surgeon to H. R. H. the Duke of York and Surgeon-General to his Majesty's Royal Navy; the other to Mr. Thos. Hobbs, Chirurgeon, in London."

In the reign of Charles II a Plymouth practitioner praises the varied virtues of the oxidized oil of turpentine as "the best, if not the only, styptic in the time of John Hunter." [5]

The resin,—that is, the oxidation products of pines and firs,—was known to the ancients. Kopp, in his "*Geschichte der Chemie,*" 1874 vol. 1, p. 392, says that the essential oils of turpentine were known to Marcus Græcus, who termed them "Aqua ardens."

In "*Die Ætherische Œle,*" by Gildemeister and Hoffman, it is stated that "the oils obtained by the distillation of the oleoresins of various Abietinceæ were known to the ancients as "πισσε ευν," and later became known as turpentine oil, which name seems to have been introduced during the period of Greek civilization.

The early observations made in connection with oil of turpentine which had been exposed to air mostly concerned its behavior at low temperatures. Margueron in *Journ. de Chim. et de Phys.*, 1794, t. 2, p. 178, states that the oil solidifies into a crystalline mass when reduced to a temperature of—22° R.

Already in 1727 I. Joseph Geoffrey had observed crystals in the neck of the retort when distilling oil of turpentine. These needle-like crystals, which were without doubt pinol hydrate, were then called "turpentine camphor."

In an abstract of a paper by Theophilus Thompson, M.D., in *Roy. Med. and Chir. Soc. Proc.*, vol. 3, London, 1858–61, p. 106, entitled "Observations on the Medical Administration of Ozonized Oils," the author describes the results obtained from the administration of ozone in association with oils; the oils being ozonized by exposure for a considerable time to the direct rays of the sun after having been saturated with gaseous oxygen according to the process of Mr. D. Campbell.

Fourteen consumptive patients were subjected to this treatment

[5] *Med. Times and Gaz.*, London, 1875, vol. 1, p. 414.

and the cases were described in detail by the author. He arrived at the conclusion that "the administration of ozonized oils has a remarkable tendency to reduce the frequency of the pulse." He goes on to say: "If ozonized oil can reduce the rapidity of the circulation—a feature of great prominence in phthisis—this remedy possesses a most valuable property, rendered still more valuable by its contributing at the same time to improve the general health." The author makes a special point of having used ozonized oil of turpentine with marked and prompt advantage in some cases of hæmoptysis.

In the same journal, same year, p. 330, Dr. E. Symes Thompson, son of the doctor quoted above, gives the results of some experiments of the effect produced on the pulse by use of ozonized oils. He records the cases of seventy patients to whom ozonized oils were administered with good effect. He draws special attention to the importance of these experiments in their relation to the treatment of phthisis, since, as he says, "anything that could retard the excessive rapidity of the vital changes would likewise check the development and progress of the disease."

He mentions several remedies that had been used to this end, all greatly inferior to the ozonides, for those, unlike the other remedies in their action, also did not exert a depressing influence on the health, but rather a strengthening and invigorating one. The author also alludes to a paper published in 1860 by a French physician "On the Use of Ozonized Oil of Turpentine in Hæmoptysis," in which the suggestions made by his father in 1859 had been followed with good results.

In a letter to the *London Medical Times and Gazette,* 1875, vol. 1, p. 25 and following, Dr. Thomas Wood, of Wilmington, N. C., says: "I would like to make a remark upon the influence which the turpentine distilleries have upon the town in which I live. Wilmington, N. C., the town spoken of, is the great export market for oil or spirits of turpentine. . . . During the late Civil War all the turpentine distilleries were closed and not put into operation again until from 1866 to 1870.

"It had long been a popular theory that the health of the community was due to the resiniferous odors from these stills, and this opinion was shared by medical men also. In 1862, after the ceasing of the operations of these distilleries, a violent epidemic of yellow fever broke out. . . . True to the theory as to the health-giving virtues of the resin and other products of the pine tree, barrels of resin were burned day and night in the streets. The only other nota-

ble epidemic was that of spotted fever, which broke out in 1865, before the operations of the stills were recommenced. Previous to the establishment of the distilleries in our midst malarial fevers were very rife, but since that time they prevail to much less extent.

"Another fact bearing a relation to the above statement is that during the Civil War, when quinine was scarce, the Surgeon-General of the Confederate States ordered experiments to be instituted at several of the large military forts to prove whether or not oil of turpentine applied to the body by means of a broad band saturated with it and worn around the abdomen had any effect in cutting short the paroxysms of ague. Its effects were described as 'marvelous' and endorsed by many observers."

In "The Medical and Surgical History of the War of the Rebellion," Washington, 1879, issued by the United States War Department, it is stated: "During our Civil War the oil of turpentine was pretty extensively employed in the treatment of flukes."

In speaking of the treatment of remittents this book says: "Turpentine emanations were frequently used in the diarrhœa accompanying these cases," and in the chapter on continued fevers it is stated: "Turpentine was extensively used."

In the splendid work, "Treatise on Therapeutics," New York, 1880, vol. 3, by Troasseau and Bindome, the treatment with the oxypinenes are recommended for the following complaints: rheumatism, vesical catarrh, diabetes, diarrhœa, neuralgia, hemorrhages, iritis, amenorrhœa, and for all disinfectant purposes.

L. S. Pilcher, in his book "The Treatment of Wounds," New York, 1883, recommends the "washing of wounds with turpentine preparations immediately before the first incision," when preparing the skin for an operation.

In Billrath's work on "Surgical Pathology," 1871, p. 31, the use of turpentine is strongly recommended for the treatment of wounds, because it is "capable of exciting a peculiarly energetic contraction of the divided capillaries."

H. C. Wood, in his celebrated treatise on "Therapeutics: Its Principles and Practice," New York, 1883, states that certain preparations of turpentine containing ozone or antozone have been recommended in medicine.

Dr. W. Gilman Thompson, in the *Medical Record,* March 3, 1894, says: "The very great value of peroxide of hydrogen and other

ozonizing preparations as local antiseptics and cleansing agents are freely admitted. It is abundantly proved by constant clinical experience and record."

In a pamphlet by Dr. Cyrus Edson "Hydrogen Peroxide in Contagious Diseases," 1893, he recommends the free administration of hydrogen peroxide, both by the stomach and intestinal irrigation. He says: "It is my opinion that this treatment will prove to be *par excellence* the treatment for cholera morbus, dysentery, typhus and typhoid fevers. As oil vehicles may carry as high as twenty-five volumes per cent. of ozone, it is obvious that they likewise may be effectually employed in the same diseases."

Dr. W. J. Morton, in an article in the *New York Medical Journal,* June 23, 1894, entitled "Ozone and its Uses in Medicine," says: "That oils absorb ozone in very large quantity and part with it slowly indeed, requires no special corroboration, since it has been well known for a long time. The combination is not an oxidation, as one might expect, but the ozone is taken up by the oil as O_3 and yielded up as O_3. The oil preparations give up their ozone when taken internally, and equally so when applied to ulcers, diphtheritic membranes, and whenever a wound dressing is required. It is noted that ozonized oils relieve pain more quickly than if they did not contain ozone."

Of course we know now that the ozone is not given up as O_3 but as H_2O_2, when the ozonide comes into contact with moist animal tissues, but this does not in the least detract from Dr. Morton's conclusions, which strongly bear out the contention that when pinene ozonide is decomposed in contact with animal tissues the intermediary oxypinenes formed have a greater therapeutic value than oil of turpentine itself.

Sir William A. Tilden, in "The Chemical History of the Terpenes," [6] states: "A few of the derivatives of turpentine were known to chemists long before they were able to determine their composition. Nearly two hundred years ago terpene hydrate was described, and as early as 1803 hydrochloride was obtained by passing hydrogen chloride gas into turpentine oil."

Since 1885 the number of researches into the character and reactions of the terpenes has greatly increased. The most important contributions to our present advance state of knowledge of these

[6] *Science Progress in the Twentieth Century,* vol. 6, London, 1912, pp. 46–61.

compounds are those of O. Wallach,[7] A. von Baeyer,[8] and W. H. Perkins, Jr.[9]

In conclusion I will only quote Lewkowitzck's classical work, published in 1909, "Chemical Technology and Analysis of Oils, Fats and Waxes," vol. 3, p. 139: "Oil of turpentine absorbs oxygen from the air (this is termed 'auto-oxidation'), and, judging from the iodine value, oil of turpentine should be able to absorb two molecules of oxygen. Whether these are present in the form of oxygen or ozone does not appear settled yet. The oxygen is 'activated' by the oil of turpentine (and contained in old oil of turpentine to a considerable extent)."

His doubts—as pointed out in my previous article on this subject—have been entirely dispelled by the splendid work of Harries and his pupils.

From the standpoint of a mere chemist it seems that an ozonide of pinene prepared from pure pinene and freshly-generated ozone would be an ideal therapeutic agent. When such a compound comes in contact with a moist animal tissue hydrogen peroxide is gradually and slowly developed, and the intermediary oxypinenes (the aldehydes and ketones) are generally conceded to have greater therapeutic value than the too active turpentine itself.

WINE OF BEEF AND IRON.[1]

By George M. Beringer.

The formula in the National Formulary, Third Edition, for wine of beef and iron has been the subject of considerable criticism. The manipulation directed is both wasteful of time and alcohol, and, withal, does not yield a preparation that is stable. Copious and continued precipitation which affects both the proteid and iron content of the preparation takes place. Moreover, shortly after making it not infrequently happens that gas develops, and often this is in sufficient quantity to burst the bottles. I have attributed this to fer-

[7] *Annalen*, vol. 225 and following.

[8] *Berichte*, vol. 26 and following.

[9] *Chem. Soc. Transactions*, 1904 and following.

[1] Presented at the meeting of the New Jersey Pharmaceutical Association, Spring Lake, N. J., June 15–18, 1915.

mentation due to insufficient alcohol in the sherry wine directed to act as a preservative.

As wine of beef and iron is of considerable commercial importance, a circular letter was directed to the principal pharmaceutical houses, inquiring if they had found the N. F. formula satisfactory; if not, what were the difficulties or defects, and requesting suggestions for improvements. The answers received from a number of these manufacturers show that their experience with the N. F. formula was similar to my own, and that an improvement in the formula was absolutely necessary.

In the course of correspondence, Dr. John M. Francis, of Detroit, has advanced an ingenious explanation as an opinion as to the cause of the decomposition. He attributes the decomposition to the ferric salt (tincture ferric citro-chloride directed in the formula). He writes:

"I am not prepared to recommend the use of ferric chloride or ferric citro-chloride; in fact, I would not recommend the use of any *ferric* salt in this or similar preparations, for the simple reason that where a ferric salt is associated with citric acid chemical decomposition will take place on exposure to sunlight or a very bright light, resulting in a reduction of the ferric salt and the formation of carbonic acid gas, which sometimes is present in sufficient quantity to blow the cork or burst the bottle."

"It took us some little time to figure out this reaction, as we supposed that the gas produced was due to fermentation. We are fully convinced now that it is a chemical reaction brought about by light." He recommends the use of the soluble citrate of iron to replace the tincture ferric citro chloride.

In a subsequent communication Dr. Francis writes:

"Our conclusion is that, regardless of which particular one may be employed, any ferric salt will decompose in beef, iron and wine to a greater or less extent when exposed to bright light, with the consequent formation of gas which is liable to blow the cork or burst the bottle. If the beef, iron and wine is made very nearly neutral a product can be manufactured which will meet all practical purposes, as very little gas is produced, even in severe conditions. If one uses ferric chloride or the tincture of ferric citro-chloride or ferric citrate and has *an excess of acid in the beef, iron and wine,* the formation of gas and the danger of explosion will increase in direct proportion to

the amount of free acid present. The best and safest plan would be to use a ferric citrate and to reduce the free acid to a minimum."

Manufacturer S—— responded: "We have not found it very satisfactory, because it continues to precipitate indefinitely."

"On June 14, 1910, we made a gallon of beef, iron and wine by N. F. method, and one gallon by simply mixing the ingredients of the formula without using alcohol. These were filtered on July 6 and again on December 14, 1910; at that time we thought the one made by N. F. method slightly better than the other, but on examining them at this time (11/11/11) we find both have heavy precipitates."

"There may be some beef extracts on the market which would cause less precipitation than the others, but all that we have tried have given this trouble."

Manufacturer L—— replied: "We have had to virtually abandon the marketing of this preparation owing to—

"*First.* It does not meet the revenue requirements as to nitrogen content. This may be due to the rather high alcoholic percentage, approximately 25 per cent."

"*Second.* There is a copious precipitation which soon renders the preparation unsightly, and the profession will not accept it, sending it back to the manufacturer about as fast as it can be sent out."

"Evidently the preliminary treatment in the N. F. of adding alcohol to the solution of beef extract, filtering and distilling off the alcohol, is given for the purpose of avoiding subsequent precipitation in the finished product. Whether it accomplishes this I am unable to say definitely, but my impression is that it does not. However, it does cause such a loss of albuminous material that the product falls short of the revenue requirement for nitrogen, and consequently it should be omitted or modified."

The above abstracts from correspondence with some of the large manufacturers show conclusively the necessity for a formula that will overcome the defects in the present N. F. formula. Without going into all of the details of my experiments, the conclusions only are here presented:

The preliminary treatment precipitates out considerable proteid matter and removes only a portion of the sodium chloride. It has no

effect in preventing subsequent precipitation. It is wasteful of time and alcohol and is unnecessary. In a good grade of beef extract the sodium chloride present and entering into solution in the wine of beef is not objectionable.

On the addition of a ferric salt, either the tincture of citrochloride of iron or the ferric and ammonium citrate, (the latter being the salt originally used and still preferred by many manufacturers), there is produced at once a brown precipitate containing iron, and, even after filtering, further precipitation continues to form with reduction in both iron and proteid content. This precipitation is not influenced by the preliminary treatment and occurs if this direction be followed or omitted.

It was found that this precipitate was largely organic salts of iron, probably the albuminate, with, at times, some peptonate, and that on adding sodium hydroxide or ammonia water to neutral or just alkaline reaction to litmus paper the precipitate very largely redissolved, and, further, that if the preparation be then filtered, further precipitation did not occur if alcohol was present in sufficient amount to prevent fermentation.

The sherry wine is usually decidedly acid, and the amount of alkali needed to obtain neutrality is larger than one would expect. Either sodium hydroxide or ammonia will answer equally well for neutralizing, but the latter is preferred, because an excess is more readily detected.

The present N. F. formula yields a preparation containing only from 13 to 15 per cent. of alcohol. This varies with the thoroughness with which the alcohol is distilled off in the preliminary treatment and the loss of alcohol occurring at the same time and also with the alcoholic content of the sherry wine added, which commonly is from 18 to 20 per cent. It was found that the decomposition did not occur if the alcoholic content in the finished preparation was increased to not less than 20 per cent.

125 Cc. of syrup likewise appears as excessive, and this can be reduced to 100 Cc. without affecting the palatability. The quantity of extract of beef now directed, 33 Gm., can be rounded off to 30 Gm., or approximately 3 per cent.

Based on these facts and experiments, I submit the following improved formula for wine of beef and iron:

VINUM CARNIS ET FERRI.

Wine of Beef and Iron.	Beef, Wine and Iron.
Extract of beef	30 Gm.
Water, hot	60 Cc.
Iron and ammonium citrate	10 Gm.
Syrup	100 Cc.
Alcohol	50 Cc.
Compound spirit of orange	1 Cc.
Ammonia water, a sufficient quantity,	
Sherry wine, a sufficient quantity,	
To make	1000 Cc.

Dissolve the extract of beef in the hot water, add the syrup and then the compound spirit of orange and alcohol previously mixed. Dissolve the iron and ammonium citrate in 750 Cc. of sherry wine, and add this solution to the other mixture, then add sufficient ammonia water to make the solution neutral or only very faintly alkaline to litmus paper, then add sufficient sherry wine to make 1000 Cc. If acid, now add, drop by drop, ammonia water until neutral or very faint alkaline reaction is obtained. Set aside for two days and then filter.

On June 25, 1912, a type sample of wine of beef and iron for the N. F. Revision was made by the above formula. An eight-ounce bottle of this has been kept under observation since that date. For a time it was kept in the cellar, and has more recently been in the laboratory, subjected to the varying changes of temperature and more or less exposed to the light. At this date, nearly three years after preparation, it is still clear, free from precipitation, and is entirely satisfactory.

INVERSION OF CANE SUGAR IN SYRUPUS.[1]

By JOSEPH L. MAYER.

In the February, 1902, issue of the *Druggists' Circular* (page 27), in an article, "Fallacious Tests for Glucose in Cane Sugar Syrup," I showed that syrupus made according to the official formula by the hot process did not contain more than a very faint trace of reducing

[1] Read before the New York State Pharmaceutical Association, June 29, 1915.

sugar, but, after being stored for five months in a corked bottle which had been placed in a cool, dark place, yielded a very heavy precipitate of cuprous oxide when tested with Fehling's solution, indicating that much of the cane sugar had been inverted.

The tests made at that time being qualitative only, the thought occurred to me recently to make a series of quantitative tests to determine exactly how much of the cane sugar was converted into reducing sugar, and the following work was therefore undertaken.

On January 28, 1915, 1000 Cc. of syrupus were made, following the directions on page 435 of the U. S. P. VIII for the cold percolation process, and the same day 1000 Cc. of syrupus were made by the method on page 435 of the U. S. P. VIII for the hot process, each sample being placed in a sterilized glass-stoppered bottle.

The syrup made by percolation had a specific gravity of 1.3148 at 25° C., and the sample made by the hot process had a specific gravity of 1.3126 at 25°.

A quantity of syrup from each bottle was immediately weighed in tared 100 Cc. graduated flasks and water added to make 100 Cc., and the reducing sugar in 50 Cc. of this solution determined by the following method of Walker and Munson:

(1) Preparation of Solutions and Asbestos.

(*a*) Solutions.—Use solutions (a) and (b) and (c) as given on page 42, under Soxhlet's modification of Fehling's solution.

(*b*) Asbestos.—Prepare the asbestos, which should be the amphibole variety, by first digesting with 1 : 3 hydrochloric acid for two or three days. Wash free from acid and digest for a similar period with soda solution, after which treat for a few hours with hot alkaline copper tartrate solution of the strength employed in sugar determination. Then wash the asbestos free from alkali, finally digest with nitric acid for several hours, and, after washing free from acid, shake with water for use. In preparing the Gooch crucible, load it with a film of asbestos one-fourth inch thick, wash this thoroughly with water to remove fine particles of asbestos; finally wash with alcohol and ether, dry for thirty minutes at 100° C., cool in a desiccator, and weigh. It is best to dissolve the cuprous oxide with nitric acid each time after weighing and use the same felts over and over again, as they improve with use.

(2) DETERMINATION.

Transfer 25 Cc. each of the copper and alkaline tartrate solutions to a 400 Cc. Jena or Non-sol beaker and add 50 Cc. of reducing sugar solution, or, if a smaller volume of sugar solution be used, add water to make the final volume 100 Cc. Heat the beaker upon an asbestos gauze over a Bunsen burner, so regulate the flame that boiling begins in four minutes, and continue the boiling for exactly two minutes. Keep the beaker covered with a watch-glass throughout the entire time of heating. Without diluting, filter the cuprous oxide at once on an asbestos felt in a porcelain Gooch crucible, using suction. Wash the cuprous oxide thoroughly with water at a temperature of about 60° C., then with 10 Cc. of alcohol, and finally with 10 Cc. of ether. Dry for thirty minutes in a water oven at 100° C., cool in a desiccator, and weigh as cuprous oxide.

N. B.—The number of milligrammes of copper reduced by a given amount of reducing sugar differs when sucrose is present and when it is absent. In the tables following, the absence of sucrose is assumed, except in the two columns under invert sugar, where one for mixtures of invert sugar and sucrose (0.4 gramme of total sugar in 50 Cc. of solution) and one for invert sugar and sucrose when the 50 Cc. of solution contains 2 grammes of total sugar are given, in addition to the column for invert sugar alone (U. S. Dept. of Agr., Bur. of Chem., Bull. 107, rev., pages 241 and 242).

The cold percolation process sample contained 0.174 per cent. invert sugar.

The hot process sample contained 0.138 per cent. invert sugar.

The cane sugar from which the syrups were made was tested by the same method and contained 0.111 per cent. invert sugar, thus indicating that in the process of making the samples very little inversion had taken place.

The syrups were then placed in a cool, dark place, samples being taken from them at frequent intervals and tested, with the following results:

	Cold	Hot	
January 28, 1915 (the day the samples were prepared)	0.174%	0.138%	invert sugar
February 10, 1915	0.172%	0.171%	invert sugar
February 25, 1915	0.292%	0.170%	invert sugar
March 9, 1915	0.559%	0.401%	invert sugar
March 23, 1915	1.123%	1.061%	invert sugar
April 2, 1915	1.807%	1.595%	invert sugar

April 9, 1915.....2.029% 1.905% invert sugar
April 15, 1915.....2.367% 2.354% invert sugar
May 6, 1915.....3.411% 3.566% invert sugar
May 19, 1915.....4.978% 4.735% invert sugar
June 3, 1915.....6.586% 5.751% invert sugar

These remarkable results not only disprove the statement very frequently made that in making syrupus by the hot process much of the sugar is inverted, a statement which my original article above referred to disproved, but they also conclusively show that making the samples by either the cold or hot process practically no inversion takes place. They show that, upon standing, the sugar in both samples become inverted, the inversion being greater in the cold-process syrup than in that where heat is employed in the manufacture.

I am still at work on the samples and hope in my next paper on the subject to report further results of the investigation.

Research and Analytical Department, Riker Laboratories.

A MEDLEY.[1]

By GEORGE M. BERINGER, JR., P.D.

Few men have so many problems and difficulties presented to them in their daily work as does the pharmacist. Accidents happen, preparations go wrong, materials are spoiled or rendered unfit for further use, by what, to the casual observer, would seem the sheer perversity of the things themselves. To him who yields without struggle to such conditions, life is but "an empty dream." To him who, by the application of some almost insignificant bit of knowledge, conquers them, there comes the wild joy of wresting from an apparent defeat an assured victory.

An illustration is furnished by a happening of a few months ago. A barrel of potassium bicarbonate, of German manufacture, had been on hand for some time. It was lined with parchmentized paper. Through some defect in the manufacture of the paper or the action of the salt upon it, the paper began to disintegrate. The more one tried to separate the salt and the paper the more they mixed. A boy was put to work spreading it on a table and picking out the

[1] Presented at the meeting of the New Jersey Pharmaceutical Association, Spring Lake, N. J., June 15–18, 1915.

bits of paper. It looked all right, but the first pound sent out was returned in a hurry. The paper was still there.

With the facilities at hand, recrystallization was out of the question, but nearly two hundred pounds of material could not be wasted, especially in the face of a rising market. Then came the magic inspiration of the electric fan. A small fan was set awhirl at one end of a long, narrow table. The table was covered with clean, heavy paper, and along the edges was placed a row of wooden boxes to prevent the potassium bicarbonate from rolling to the floor. The end was left open.

Through the swift current of air, passing along this narrow channel, the material was allowed to drop, a handful at a time. Away went the paper—big bits and little bits—in a merry whirl, while the heavy chemical, bright and clean, dropped on the table, freed from its troublesome companion. Scarcely a pound of material was lost.

How do you clean capsules after you have filled them with powdered material? Do you wipe them on the towel at the prescription counter—whether that towel is clean or otherwise? Well—don't confess what you do—just try this. Take a piece of absorbent gauze of such size that it can be folded into a square of eight or ten inches, having four thicknesses of material. Place the capsules to be cleaned in the centre of this. Gather up the corners and edges of the gauze square into one hand, in such a manner that the capsules are suspended in a loose bag. Now rub this bag across the palm of the other hand a few times, pressing firmly. Each capsule is rubbed between the layers of gauze, and every particle of powder is removed, leaving it bright and clean.

You are in a hurry for some camphorated oil. You crush the camphor into coarse lumps and throw it into the oil, put the mixture on a water-bath for an hour or so, and return to find lumps of camphor still in evidence. Then, if you are of that temperament, there follow a few splutters, dashes, blanks, and exclamation points, but the camphorated oil is still unfinished. Before you try it again, go to your hardware dealer and spend from 75 cents to $1.25 for an almond grater. Put your camphor into this machine, a few lumps at a time, turn the handle, and have the camphor in an almost uniformly fine granule. Add this to your oil. Put it on the water-bath and have your preparation—less the dashes, etc.—in fifteen minutes.

Speaking of the almond grater, you will be surprised at the

number of uses you will find for it. You can granulate castile soap for making soap liniment; you can granulate opium, if you make preparations of that drug; and you can granulate almonds and make your almond meal from real almonds.

THE NUMBER AND KIND OF DRUG ADDICTS.[1]

By M. I. WILBERT, Washington, D. C.

In recent years social workers, reformers, and newspaper writers generally have vied with each other in the presentation of startling data regarding the number and kind of drug addicts in this country. In doing so they have established the general impression that those engaged in the various branches of medicine, and particularly those engaged in the practice of pharmacy, have been delinquent in that they have failed to safeguard the sale and distribution of habit-forming drugs with the care that properly should have been exercised.

Among the statements frequently met with in current papers and periodicals the following are representative:

"More than two per cent. of the people of this country are addicted to the use of opium and cocaine, and this number is being augmented at the rate of 100,000 a year."

"Fully ninety per cent. of the opium we import is used for illegitimate purposes."

"For every ounce of cocaine employed legitimately there are 200 ounces consumed illegitimately."

"Physicians are responsible for at least ninety-five per cent. of the habitual users of opium, its compounds and alkaloidal salts."

"More dope fiends have been created by the refilling of prescriptions than in any other way."

"At least ten per cent. of the 45,000 drug stores in the country exist largely upon the illegitimate sale of habit-forming drugs."

"Many of the proprietary remedies sold to the laity contain a sufficient amount of dope to develop and to maintain a drug habit."

"The use of heroin as a 'kicker' in patent medicines is comparatively common."

"The Harrison law, excellent so far as it goes, is effectively

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[1] Presented at the meeting of the Pennsylvania Pharmaceutical Association, Forest Park, Pa., June 22–24, 1915.

negatived by the exceptions included in Section 6. The most exacting dope fiend could not ask for a larger hole in the law. If he can get an unlimited amount of his favorite drug in a nostrum form, anything else that the Harrison or any other law may or may not provide is a matter of indifference to him."

As has been pointed out before,[2] some, at least, of these statements are not based on reliable data, while others, having the elements of truth, are misleading, either because of their incompleteness or because of the partial misstatement of fact. While it is unfortunately true that the number of drug addicts in the United States is disgracefully large, it does not, and of necessity can not, even approximate the maximum that has been stated.

Practically all of the opium and coca used in this country is imported through legitimate channels, and because of the comparatively high import tax considerable care is exercised to insure the reporting and recording of all of the product at our disposal, so that we have fairly reliable data on which to base an estimate of the amount of either drug that is available for all purposes.

Converting the recorded quantities of the several drugs imported into average doses, as presented in the Pharmacopœia of the United States, we find that for some years the total amount of these drugs imported has been fairly uniform and will aggregate an average of approximately 2,500,000,000 doses of opium, its derivatives and alkaloids, and 325,000,000 doses of coca leaves and cocaine. These figures serve to definitely fix the amount of available material, and, quite regardless of the proportion of the several drugs that may be used legitimately or illegitimately, the sum-total of illegitimate use cannot well exceed the sum-total of the available material.

A rather interesting source of information regarding the actual number and kind of drug addicts is available through the enforcement of the Tennessee anti-narcotic law of 1913. Lucius P. Brown, the State Food and Drugs Commissioner of Tennessee, in a recent report[3] says that after twelve months of operation there were registered in the State of Tennessee under the provisions of the anti-narcotic law 2370 persons of all ages and years These included 784, or 33.1 per cent., males and 1586, or 66.9 per cent., females.

The average consumption per day of the morphine addicts was 8.5 grains, or approximately 1000 doses each month, or 12,000 doses

[2] P. H. Rep., 1914, vol. 29, p. 3180.

[3] *Am. J. Public Health,* 1915, vol. 5, pp. 323 and 333.

a year. The State of Tennessee contains slightly more than two per cent. of the total population of the United States, and, on the supposition that the same ratio of addicts and the amount of material consumed will hold good throughout the country, we would have a total of something more than 118,000 drug *habitués* consuming approximately 1,416,000,000 average doses per year.

Granting the somewhat improbable assertion that ninety per cent. of the opium imported is used illegitimately at the rate that it is said to be consumed in the State of Tennessee, we could have as a maximum not more than 187,000 users of opium, its derivatives and alkaloids, in all parts of the United States.

In regard to the use of cocaine, a recent authority asserts that one ounce of cocaine is enough to keep fifty fiends thoroughly well doped for a week, or, in other words, that one ounce of cocaine is enough to keep one fiend thoroughly well doped for a year.

Granting that all of the vailable 150,000 ounces of cocaine were used illegitimately, there could be, at this rate, a total of 150,000 cocaine fiends in the United States.

That this estimate is somewhat high would appear from the report by C. G. Steinmetz, Jr.,[4] who made a study of fifteen cases of cocaine habit acquired by men employed where the drug was manufactured. The daily quantity taken varied from twenty to sixty grains; the method of taking was solely by snuffing it. Even on the basis of the lower quantity the consumption per annum would be in the neighborhood of fifteen ounces and thus reduce the possible number of cocaine fiends very materially.

Pharmacists who have been unfortunate enough to meet with patients addicted to the use of cocaine will appreciate that the figures given by Steinmetz are much more nearly in accord with actual practices than are the figures previously quoted. Taking all the available facts into consideration, it would appear that the estimate made by the committee of the American Pharmaceutical Association, some years ago, that the drug addicts in this country do not exceed 200,000 in number is approximately correct even at the present time.

That other previously-made estimates of the number of drug addicts in this country were altogether erroneous is further evidenced by the published reports on hospital admissions since the Federal anti-narcotic law came into effect. It had been predicted that the result

[4] *J. Am. M. Assoc.*, 1915, vol. 64, p. 1271.

of the enforcement of this law would be a besieging of hospitals by drug addicts and a crime wave of national scope, accompanied by a trail of suicide and death. While the effect of the enforcement of the Federal anti-narcotic law has been clearly evidenced by hospital reports, the results have been by no means so far-reaching or so startling as had been expected.

The most shocking of the several available reports is that of Wm. D. McNally, Coroner's Chemist, Cook County, Chicago,[5] who states that during the month of March seven deaths occurred in Cook County that were indirectly due to the sudden cessation of the use of morphine. Four died from taking an overdose of morphine. One of the four died from taking an overdose of "Dr. Weatherby's Remedy," a morphine cure containing over seventeen grains of morphine sulphate per ounce. During the month of December, 1914, not a single death occurred in Cook County from morphine. During January and February the record shows one death for each month.

Clifford B. Farr [6] reports that since the enactment of the Harrison law the number of admissions to the Philadelphia General Hospital of cases of morphine and heroin addiction has markedly increased. In the first sixty-eight days of 1915, eighty-six patients addicted to heroin were admitted, while in 1911 there was not one.

Other cities have reported similar results, but, so far as known, the amount of suffering has not in any way measured up to the results that were predicted by newspaper writers and others when the Federal anti-narcotic law was under consideration.

Now just a word in regard to the origin of drug addiction. C. E. Terry, City Health Inspector of Jacksonville, Fla., in the report of a study of local conditions,[7] states that of 213 cases of drug habituation studied by him personally their origins, in the order of their frequency, were as follows:

Through physicians' prescriptions or treatment personally administered, 54.6 per cent.

Through the advice of acquaintances (for the most part themselves users), 21.6 per cent.

Through dissipation and evil companions, 21.2 per cent.

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[5] *J. Am. M. Assoc.*, 1915, vol. 64, p. 1264.
[6] *J. Am. M. Assoc.*, 1915, vol. 64, p. 1270.
[7] *Am. J. Public Health*, 1914, vol. 4, p. 32.

Through chronic and incurable disease, 2.4 per cent.

The conclusions reached by Terry agree very well with those enunciated by Brown, that from ninety to ninety-five per cent. of the persons habitually using narcotics do so entirely unnecessarily.

It should be remembered that the figures quoted above refer solely to the number and kind of addicts, generally recognized as such, who use narcotic drugs in comparatively large amounts. There is still another, and a very pathetic, side to the drug addict problem that has as yet received altogether too little attention. This problem involves the ways and means of generating the habit and also includes a consideration of the unfortunates who for one reason or another feel compelled to continue the use of comparatively small amounts of a narcotic drug.

Practically all authorities are agreed that the continued use of cocaine is a vice rather than a disease, and the Federal, as well as State, anti-narcotic laws appear to recognize this fact and provide special safeguards to prevent the indiscriminate sale or distribution of even small amounts of cocaine or of preparations containing it.

With opium, morphine, and related products, on the other hand, no such precautions have been taken, despite the fact that addiction to the use of these things is generally recognized as a condition over which the individual patient has little or no control.

Up to the present time altogether too little authoritative information is available regarding the origin and subsequent progress of the condition commonly described as morphinism, because physicians usually see only the fully-developed cases or the, at times, spectacular end results.

The morphine or opium addict, as a rule, is secretive and generally seeks relief in ways that are destined to make him an easy prey for the charlatan or advertising quack who promises a positive cure with secrecy.

Lambert, Towne, and others who have made a study of drug addiction agree with the conclusions of Terry, quoted above, that a very large proportion of the persons addicted to the use of opium and its alkaloids have acquired their habit from the thoughtless renewal of prescriptions containing narcotics or by self-medication with preparations containing comparatively small quantities of an opiate.

In this connection it may be said that it is not generally realized

that the taking of even small doses of opium or morphine, at regular intervals, for a continued length of time will be more likely to develop the opium habit than the occasional indulgence in large quantities.

It has been asserted [8] that the average person will develop an addiction to opium or one of its alkaloids after thirty days of daily use, and that after the continued use of such a drug for three months or more it is practically impossible to discontinue its use without medical aid.

With these several possibilities fairly well established, it would appear to be unfortunate to endorse or even to countenance exception clauses in anti-narcotic laws, such as Section 6 of the Federal law, which permit of the indiscriminate sale or distribution of preparations that not alone may, but positively will, establish a habit that, once established, cannot readily be overcome.

In the Federal anti-narcotic law we have the possibility of an accurate survey of existing conditions in connection with the use and abuse of certain narcotic drugs. The findings, if they can be made a matter of record, will place the blame for the illicit use of the proscribed drugs where it rightfully belongs, and will suggest ways and means for correcting existing abuses.

To secure efficient restrictions on the sale and distribution of narcotics, and to demonstrate that they are not primarily to blame for the generation and continuation of the addiction referred to, pharmacists individually should not alone be willing to comply with existing requirements under the law, but should see to it that others engaged in the same line of business comply fully with the spirit as well as the letter of existing laws and regulations.

There can be no gainsaying the fact that the amounts of opium and of coca consumed annually in this country are out of all proportion to the actual need for medicinal purposes, but to locate the existing leaks the followers of all branches of medicine, and particularly the men engaged in the practice of pharmacy, must make consistent and persistent efforts to purge themselves of even the suspicion of being directly or indirectly to blame for existing abuses.

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[8] Pettey, G. E., *J. Am. M. Assoc.*, 1913, vol. 61, p. 566.

THE CULTIVATION OF MEDICINAL PLANTS.[1]

By Dr. Fred. B. Kilmer, New Brunswick, N. J.

(*Continued from page 359.*)

Botanic Gardens.

A review of the World's Botanic Gardens, by Prof. Albert Schneider (Amer. Jour. Pharm., January, 1904, 1–30), points out the significance and value of such gardens to the progress of pharmacy and medicine.

From this review we learn of the mythical gardens of antiquity and tradition, including the Garden of Paradise and the Royal Gardens of Egypt and Rome. From this article it appears that as early as 1545 medicinal herbs were cultivated in the Italian gardens at Padua. The "Jardin des Plants" of Paris, founded in 1610, added millions of dollars to the wealth of the French nation. The "Jardin Botanique de la Faculty la Medicine," which is a part of this garden, is the largest and most complete garden of medicinal plants in the world.

France, England, Germany, Austria, Italy, Holland, Russia and the United States have extensive botanic gardens in which, to some extent, medicinal plants are cultivated. The list of botanic gardens in the United States is given as follows: New York Botanic Gardens; Shaw Botanic Gardens, St. Louis; Philadelphia Botanic Gardens; Ann Arbor, Mich.; Indiana State University; San Francisco, California.

Prof. Schneider suggests a co-operative agreement among the authorities of these different gardens as to the scope of the work done by each.

So far the American Botanic Gardens have done but little in the way of cultivation of medicinal plants that can be considered as of economic value. Their work in general is limited to other problems. The resources of these gardens could be made of great value for the furtherance of this work. To bring it about would require requisite funds and intelligent direction.

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[1] Read before the National Association of Manufacturers of Medicina Products, Waldorf-Astoria Hotel, New York City, February 8, 1915.

Factors in Drug Plant Production.

The following note by W. W. Stockberger summarizes the situation from the agricultural point of view, and incidentally throws an important light upon the whole problem:

The first essential for successful drug plant production on a commercial scale is the existence of a market for the product. For some crude drugs the demand is constant and steady, while for many others it is variable, or exceedingly limited. In the case of drugs for which there is a limited demand, numerous or extensive plantings may easily result in overproduction, with a consequent decline in the market price. The prospective grower of drugs would do well to acquaint himself with the market, and to make sure that the cost of production, plus packing and shipping expenses, do not make the total cost so great that the drugs cannot be grown at a profit.

It is also essential to know that the species selected for cultivation will do well under the conditions of soil and climate existing where the planting is to be made. Drug plants vary widely in their requirements with respect to these conditions, and satisfactory yields can be expected only when the requirements of these plants are understood and properly met.

The economic situation is another weighty factor. Assuming that the soil and climate are suitable, it does not follow that drugs can be grown at a profit. They must yield returns equal to, or greater, than those from other crops which may be grown on the same land. Since much handwork is necessary in the production of most drugs, a sufficient labor supply must be readily available. The price of land, the cost of labor and the distance from market, are additional items to be fully considered before attempting to grow drugs commercially.

The prospective grower of drugs who has not had some practical experience in gardening, and who lacks a knowledge of the requirements of crude drugs, should proceed cautiously. Although some medicinal plants may be grown as easily as ordinary garden crops, others require the special knowledge and skill of the practiced gardener, if good results are to be secured. The valuable constituents of many drug plants vary in quantity, according to the time of gathering and method of drying; hence a knowledge of the right time for harvesting and the proper methods of curing is necessary for the production of drugs of high quality.

Literature on Drug Culture.

For more than twenty-five years just past, considerable literature has been published on the subject of medicinal plants and their culture. Within the past few years this literature has greatly increased and is assuming a modern and practical trend. For the convenience of those who may desire to more thoroughly study the subject a list of important references are here given. It may be noted that in addition to this list there is available extensive literature on the soil, its chemistry, fertility, tilling, etc., as well as upon seeds, seed testing, and for the student of the morphology and chemistry of medicinal plants and kindred subjects may be perused with profit. The citations here made have a more or less practical bearing upon the subject of drug culture.

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"Applied and Economic Botany," by Henry Kraemer, 806 pages, published 1904.

As among the most recent text-books which should be consulted by those interested in the study and cultivation of medicinal plants, I recommend "Applied and Economic Botany," by Henry Kraemer. (Published by the author.) This work covers the technical study of plants and plant life with special study of medicinal plants.

One chapter is devoted to the discussion of the cultivation of medicinal plants. In this section practical observations are given to medicinal plants grown from seed: "Propagation by Cutting," "Collection and Drying of Drugs," "Relative Value of Drugs from Cultivated and Wild Plants," "Progress of Medicinal Plant Cultivation in the United States." From this work the following is extracted:

"When our forests and woods were full of wild medicinal plants that could be easily gathered, there was hardly an incentive to con-

sider the farming of them. Now, that they are becoming scarcer, the need is especially apparent. Our interest in the cultivation of medicinal plants, however, is not primarily because there is a growing scarcity of the sources of supply, but in order that drugs of uniform quality and increased value may be had. Fortunately, there is a tendency on the part of some manufacturing pharmacists to concentrate their efforts upon a few drug-yielding plants and to study them in relation to their active principles throughout different periods of the season. In addition to these actual experiments, there are numerous inquiries made regarding the possibilities of the successful farming of medicinal plants.

"If one is satisfied that it is worth while to take up the cultivation of any particular plant, its geographical range should be studied, both as to where it is indigenous and where it has become naturalized. The literature should be gone over not only for facts regarding the cultivation and distribution of the particular plant in view, but also of some of the related plants.

"At the same time that these preliminary studies are made, a careful survey should be taken of the plants which are indigenous and in cultivation in the particular locality where one is proposing to locate the farm. Then, of course, everything should be done on a small scale at first. If there is no information available, then he must, on the basis of the general principles laid down for the cultivation of medicinal plants, proceed with their culture, conducting parallel experiments with propagation by both seeds and cuttings.

"Then when the crop is harvested he must, by analytical and other means, satisfy himself as to the value of his product compared with the commercial article, and with these facts in hand submit specimens and request quotations from the dealer in crude drugs, and the wholesale druggist. On this basis he will arrange for all future crops with some certainty as to their market value. Experience has shown that cultivated crops command a higher price than the drugs obtained from wild plants, even though their superiority cannot be demonstrated by analytical means. For instance, no one is trying to determine by an analytical process whether any given lot of tobacco, tea, or coffee is of superior value, and yet the competent dealer and the discriminating public even recognize the qualities of the grades that are offered. This is even more marked with the products that have been derived thus far from cultivated medicinal plants, and are appreciated by some pharmacists and physicians."

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The author corrects many misstatements which have been made in respect to the culture of medicinal plants, and believes the time has arrived for the accumulation of practical data and its circulation

under the most conservative and guarded statements. *Journal A. Ph. A.*, vol. 3, p. 34.

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This paper in a degree covers the entire subject of medicinal plants in five divisions, as follows:

Commercial samples and shipment of drugs.

Crude drug merchants.

Individuals living in or near the producing regions or others carrying on investigations of similar plants.

Public and private botanical gardens, experimental stations, and other institutions.

Commercial seedsmen and nurserymen.

The paper includes germination tests, and a list of commercial seedsmen and nurserymen from whom seeds and plants may be obtained.

The writer states that open-field methods of seeding have been found impracticable and in many cases impossible for many medicinal plants.

The author is of the opinion that more data are required upon the propagation of the most important drug plants which are adapted in this country; that methods would have to be developed to suit conditions of soil and climate and at the same time be varied to meet the purposes of the work.

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A student of this volume will certainly develop an intimate knowledge concerning drugs when taken from any point of view.

The book is most extensively and handsomely illustrated with

drawings and half tones, and under each drug is given all of the information which is available and in accordance with the brightest consideration of the subject. It is considered by those competent to judge as one of the most important books ever written upon the subject, and is a monument to the painstaking care, genius and attainments of this eminent authority. It is to be regretted that the present war will somewhat interfere with the completion of this work.

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CURRENT LITERATURE.

The Antiseptic Action of Hypochlorous Acid and Its Application to Wound Treatment.

The value of chlorine as an antiseptic and germicide has been convincingly demonstrated in recent years by its successful application in the sterilization of the water in swimming pools. It has also been demonstrated bacteriologically that very dilute solutions are efficient; without this added demonstration its practical application would be unavailable, as it is common knowledge that chlorine is decidedly irritating.

The authors of this paper directed their attention to the hypochlorites in an endeavor to find an antiseptic which could be used as a first dressing in the field to prevent sepsis.

They found, as a result of their experiments, that hypochlorous acid is a more potent germicide than its salts. In their work they tested the efficiency of this gas (1) by its action in killing or preventing the growth of organisms on artificial culture media; (2) by its

action in sterilizing infected organic matter. The acid can be used as a gas or as a solution in water. Their method of directing the gas to a wound was to mix intimately equal parts of bleaching powder and boric acid powder and apply on gauze to the infected wound; the moisture in the wound, of course, would liberate hypochlorous acid gas. A solution of the gas was also found to be of much value as a wet dressing. It was found that a one-half per cent. solution gave practically no pain and retained its potency about three weeks. The solution is most conveniently made by adding 12.5 grammes of bleaching powder to a litre of water, shaking vigorously, then adding 12.5 grammes boric acid powder and shaking again. The solution is allowed to stand over night and filtered. The clear solution is then ready for use

This solution contains:

Hypochlorous acid	0.54 per cent.
Calcium borate	1.28 per cent.
Calcium chloride	0.17 per cent.

They conclude that the gas and the solution, while extremely potent against organisms and their spores, cause little or no harm to the tissues; that the effect is purely local; the decomposition products are devoid of toxicity, and there is, therefore, no danger to be apprehended from absorption. It also has the desirable advantage of being inexpensive. (*The British Medical Journal,* July 24, 1915, No. 2847, page 129.)

JOHN K. THUM.

BOOK REVIEWS.

THE DRUGGIST AND HIS PROFITS. By Harry B. Mason. Published by E. G. Swift, Detroit, Michigan.

This excellent little book, written by Mr. Mason, who has for many years studied the financial conditions existing in the retail drug business, should be read by every druggist.

It would be difficult to study these chapters in which scientific business methods are explained and urged without even the most reluctant or pessimistic being impressed by the importance of their adoption.

The many illustrations cited from the experience of real stores show the need for better records and a more exact analysis of busi-

ness and help to bring the conviction that this is not the dream of a theorist, but the prescription of a skilled diagnostician who stands ready to cure those who will take the medicine.

It is here that the main difficulty arises: can the rank and file be persuaded to take the prescription? It is often necessary to experience serious financial problems before many can be induced to keep the necessary records. The wise man to-day is learning to avoid this difficulty by adopting a system which insures success from the start and which takes business out of the realm of chance.

It is gratifying to know that this added help, in the form of an inexpensive book, is available for the many druggists of the country who are studying and adopting satisfactory plans by which to start their business career.

E. F. C.

COLLECTED PAPERS FROM THE RESEARCH LABORATORY OF PARKE, DAVIS & Co.—Dr. E. M. Houghton, Director. Reprints, vol. 3, 1915.

The volume in hand comprises more than twenty reprints of articles involving original research. The subjects considered are chiefly of bio-pharmaceutical interest and represent the work of one year in the research laboratory of one of the largest manufacturing houses in the United States. They should be read very carefully by pharmacists and physicians, as they indicate the trend of modern therapy and the nature of the problems that confront the pharmacist. It is always gratifying to the EDITOR of this journal to review substantial work and to commend the efforts of investigators, no matter what their connections may be. Parke, Davis & Co. was one of the first of American manufacturing houses to give attention to original research, and their publications during the last twenty-five years or more have been appreciated by investigators generally. Much of the work which has emanated from this laboratory is scattered, and their present efforts in bringing the papers of their research workers into a single volume is greatly appreciated, being in convenient form and more readily accessible. No American firm has been more willing to lend its efforts to help research students in supplying them with material and information, and even in some instances have their research workers personally help in the solution of special problems.

DORLAND'S AMERICAN POCKET MEDICAL DICTIONARY. Edited by W. A. Newman Dorland, M.D., editor "American Illustrated Medical Dictionary." Ninth edition, revised and enlarged. 32mo. of 691 pages. Philadelphia and London: W. B. Saunders Company, 1915. Flexible leather, gold edges. Plain, $1.00 net; thumb index, $1.25 net.

If there is anything that is needed to have in a compact form it is a dictionary. Probably nothing will be of greater assistance to the professional man than the study of technical words and their meaning. We are all of us too prone to be superficial and careless, as regards the true meaning of words, and this can only be remedied by the constant use of a dictionary. Frequently a dictionary is too large, or it is inaccessible for ready use, but when it is small and compact, sufficiently so that it can be in pocket form and handsome enough to be kept in a drawing-room, it becomes a three-fold blessing to the owner. Dorland's American Pocket Dictionary combines all these qualifications, and no matter what other dictionaries a professional man has, if he needs to know medical terms and their meanings, he will find this a very valuable little book.

PENNSYLVANIA PHARMACY LAWS, in effect 1913-1915. Presented with the compliments of Smith, Kline & French Company, Philadelphia.

There are so many laws regulating the practice of pharmacy and allied branches in Pennsylvania that there must be considerable confusion in the minds of those engaged in the business within the State. Some years ago Mr. L. L. Walton, secretary of the Pennsylvania Pharmaceutical Examining Board, published in the *Proceedings of the Pennsylvania Pharmaceutical Association* a compilation of the pharmacy laws of the State of Pennsylvania. Using this as a basis, Messrs. Smith, Kline & French Company have added to it the more recently enacted laws, as well as other laws which have a bearing upon the conduct of the drug business. The compilation is most complete and the work will be found very valuable to all pharmacists.